REMARKS

Claims 25-30, 32-36, and 67-82 are pending in the application. Claims 1-24, 31, and 37-66 have been cancelled without prejudice. Claims 25, 28, and 32 have been amended. New claims 67-82 have been added. No new matter has been added.

Objection to the Specification

The continuing data on page 1 of the application has been updated as requested on page 2 of the Office Action.

35 U.S.C. § 112, 1st Paragraph (Enablement)

On pages 2-6 of the Office Action, claims 25-36 were rejected as allegedly not enabled.

Applicants respectfully traverse the rejection in view of the claim amendments and the following comments.

The present invention is based, at least in part, on applicants' identification and characterization of a protein that binds to LDL. This LDL-binding protein has been designated LDL Binding Protein-2 ("LBP-2"). LBP-2 is believed to be involved in the focal, irreversible binding of LDL to the arterial wall, an event that starts and sustains the atherosclerotic process (see, e.g., page 12, lines 17-21).

Amended independent claim 25 and new independent claim 71 are directed to methods for identifying a candidate agent that binds to LBP-2 by contacting *in vitro* a candidate agent and an LBP-2 polypeptide comprising an amino acid sequence that binds to LDL and (i) has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:43, (ii) is identical to a fragment of at least ten amino acid residues of SEQ ID NO:7 or SEQ ID NO:43, or (iii) differs by one or more conservative amino acid substitutions from the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:43.

The method claims of the present application have been amended to recite LBP-2 polypeptides having a scope that corresponds to the LBP-2 polypeptide and LBP-2 nucleic acid claims of the sibling applications that issued as U.S. Patent Numbers 6,632,923 and 6,878,817.

Applicants respectfully submit that the teachings of the specification, combined with the knowledge of a person of ordinary skill in the art at the time the present application was filed, enabled a skilled artisan to make and use polypeptides containing the LDL-binding fragments and variants of LBP-2 recited in the claims.

It is well within the grasp of the biologist of ordinary skill to prepare, for example, a polypeptide having at least 80%, at least 90%, or at least 95% sequence identity to the human LBP-2 of SEQ ID NO:7 or SEQ ID NO:43. The specification details standard mutagenesis methods that can be used to make amino acid sequence variants (page 19, line 2 to page 20, line 2). Furthermore, the specification instructs, and the skilled biologist is well aware, that conservative amino acid substitutions can be made in the LBP-2 polypeptide sequence so as to reduce the likelihood that a given amino acid sequence will result in a loss of LBP-2 function (page 17, line 21 to page 18, line 15). In addition, fragments of the full-length LBP-2 polypeptide can be generated by removing one or more nucleotides from one end (for a terminal fragment) or both ends (for an internal fragment) of a nucleic acid that encodes a polypeptide (e.g., page 21, line 2 to page 22, line 3). Nucleic acids that encode fragments of a polypeptide can also be generated by, e.g., random shearing, endonuclease restriction digestion, or a combination of any of these methods. Expression of such a recombinant DNA would produce the desired LBP-2 fragments.

In addition to being able to readily produce human LBP-2 fragments and sequence variants, it would have required no undue experimentation for the skilled artisan to identify those fragments or variants that retain the specific LDL binding activity recited in the claims. The specification instructs how to evaluate the ability of LBP-2 polypeptide variants and fragments to bind to LDL. For example, Example 8 describes how to perform affinity coelectrophoreses (ACE) assays that detect the binding of LBP-2 to LDL (page 47, line 23, to page 49, line 20). In addition, the experiments detailed in Example 8 indicate that a particular stretch of acidic amino acids of LBP-2 (about amino acids 329-354 of human LBP-2) participates in the binding of LBP-2 to LDL (page 49, lines 4-20). Examples 9 and 10 further detail methods for determining whether a given candidate inhibitor (such as an LBP-2 peptide fragment) blocks the binding of

LBP-2 to LDL (page 49, line 22, to page 51, line 10). By using the assays described in the specification, the skilled artisan would have been able to readily determine whether a given human LBP-2 fragment or sequence variant binds to LDL.

In light of the foregoing, applicants respectfully submit that a person of ordinary skill in the biological arts at the time the present application was filed would have been able to practice the claimed invention without undue experimentation and with a reasonable expectation of success.

35 U.S.C. § 112, 2nd Paragraph (Indefiniteness)

At page 6 of the Office Action, claim 25 was rejected "as being indefinite because it lacks essential steps as claimed in the method for identifying a candidate agent that binds to LBP-2. No method steps are recited to demonstrate the claimed effect."

Applicants respectfully submit that claim 25 does not lack an essential step. The two steps recited in the claimed method are *contacting* a candidate agent and an LBP-2 polypeptide and *measuring* the binding of the candidate agent to the polypeptide. The skilled person would readily understand that *measuring* the binding of the candidate agent to the polypeptide is the means by which the method identifies a candidate agent that binds to LBP-2.

At pages 6-7 of the Office Action, claims 25, 28-32, and 34-36 were rejected because of their use of the terms "LBP-2" and "LDL." Claim 25 has been amended to include the full, spelled-out words prior to the first appearance of each of these abbreviations. In view of these amendments, applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance.

Enclosed is a Petition for Three Month Extension of Time and a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 10797-004006.

Respectfully submitted,

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